

**Remarks**

After entry of this amendment, Claims 1-3, 6, 7, 9-23, 25-29, 32, 33, 35-50, 52-54 and 56-58 are pending in the instant application. Claims 1-3, 6, 7, 20, 22-23, 25, 27-29, 32, 33, 49, 52, and 54 have been amended, and Claims 24, 51, and 59-61 have been cancelled. Support for the amendments may be found in the specification as filed at, for example, page 13, lines 12-23 and claims 24 and 51. No new matter has been added.

Applicants acknowledge with appreciation the Examiner's entry of the previous amendments made May 2, 2005 and July 28, 2004, as well as withdrawal of two of the three previous rejections under 35 USC § 112, first paragraph. Applicants also thank the Examiner for reviewing the Information Disclosure Statement submitted May 2, 2005, and include an additional Information Disclosure Statement herewith. Upon review of the file of the application, Applicants have noticed that on the Information Disclosure Statement filed October 13, 2003, the first two references, US Patent Nos. 5,453,363 and 5,593,865 were not initialed on the returned Form 1449 (although the remaining 9 references were initialed as considered). Applicants respectfully request that the Examiner provide a copy of this Form 1449 with an indication that these references have been considered.

**Claim Rejections – 35 USC § 112**

As noted in paragraph 3 of the outstanding Office Action, Claims 1-3, 6, 7, 9-29, 32, 33, 35-54 and 56-58 are rejected under 35 USC § 112, first paragraph, because the specification, while being enabling for methods of increasing the activity of the p75 TNF receptor produced by mammalian cells by contacting the receptor with a reduction/oxidation coupling reagent at a pH of about 7 to about 11 and isolating a fraction of the preparation of the recombinant soluble form of the p75 TNF receptor with a more active conformation, does not reasonably provide enablement for that method using the p55 TNF receptor.

Solely to advance prosecution of the instant case, and without acceding as to the merits of the rejection, Applicants have amended the pending claims to recite methods involving the p75 TNF receptor. Specifically, the limitations of claims 59, 60, and 61 have been incorporated into the independent claims 1, 27, and 54 on which they depend. In addition, claims 2, 3, 6, 7, 20-25, 27-29, 32, and 33 have been amended to correct the corresponding antecedent basis for this limitation. Applicants reserve the right to pursue the cancelled subject matter in a future related application. These amendments moot this rejection, and Applicants therefore request reconsideration and withdrawal of the rejection on these grounds.

In paragraph 4 of the outstanding Office Action, Claims 27-29, 32, 33 and 35-53 are rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner notes that the phrase “the TNF-receptor” on line 2 of the claim has insufficient antecedent basis since there is more than one type of TNF-receptor. Applicants submit that this rejection has been mooted by amendment of the claim to recite “a p75 TNF-receptor”, and request withdrawal of this rejection.

#### **Claim Rejections – 35 USC § 112**

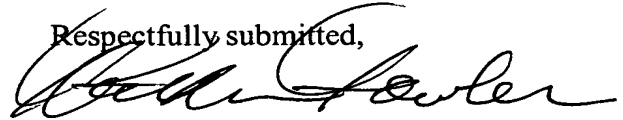
In paragraph 5 of the outstanding Office Action, Claims 1-3, 6, 7, 9-29, 32, 33, 35-54 and 56-61 remain rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that the claims do not specify what a desired or undesired conformation of a TNF receptor is or how such could be determined, and so it is not clear what is being claimed. This rejection was maintained from the previous action.

Applicants have amended the independent claims 1, 27, and 54 to make clear what the desired conformation of the p75 TNF-receptor, and how that can be determined. In particular, Applicants have amended these claims to recite the limitations “wherein the desired conformation has a higher binding affinity than an undesired conformation for a cognate ligand of the p75 TNF-receptor,” “wherein the desired configurational isomer has a higher binding affinity than an undesired configurational isomer for a cognate ligand of the p75 TNF-receptor”, and “wherein the undesired conformation has a lower binding affinity for a cognate ligand of the p75 TNF-receptor.” These limitations are derived from the language of previous dependent claims 24 and 51, which language had not been deemed indefinite. The specification describes that such affinity assays can be used to determine the desired conformation both in general (*see*, for example, page 13, lines 12-23) and by way of specific example (*see* Example 2, page 21, lines 19-34). Thus, Applicants submit that the claims specify what a desired conformation of a p75 TNF-receptor is, and how that can be determined. Accordingly, Applicants request reconsideration and withdrawal of the rejection on this basis.

**CONCLUSION**

Applicants submit that the presented claims are in condition for allowance. A favorable action is earnestly requested. Applicants' attorney invites the Examiner to call her at the number below if any issue remains outstanding.

Respectfully submitted,



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